

## SEQUENCE LISTING

<110> Merck & Co., Inc.  
Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.

<120> HCV REPLICONS CONTAINING NS5B FROM  
GENOTYPE 2B

<130> 21564Y PCT

<150> 60/517,605  
<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1  
<211> 591  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> modified NS5B

<221> VARIANT  
<222> (5)...(5)  
<223> Xaa = threonine or serine

<221> VARIANT  
<222> (24)...(24)  
<223> Xaa = asparagine or serine

<221> VARIANT  
<222> (31)...(31)  
<223> Xaa = methionine or isoleucine

<221> VARIANT  
<222> (376)...(376)  
<223> Xaa = isoleucine or leucine

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Glu Glu Glu Lys Leu Pro Ile Xaa Pro Leu Ser Asn Ser Leu Xaa Arg  
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Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg  
35 40 45  
Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr  
50 55 60  
Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala  
65 70 75 80  
Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser  
85 90 95

Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser  
     100                   105                   110  
 Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu  
     115                   120                   125  
 Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val  
     130                   135                   140  
 Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile  
     145                   150                   155                   160  
 Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr  
     165                   170                   175  
 Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly  
     180                   185                   190  
 Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp  
     195                   200                   205  
 Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe  
     210                   215                   220  
 Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr  
     225                   230                   235                   240  
 Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu  
     245                   250                   255  
 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln  
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 Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser  
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 Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys  
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 Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu  
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 Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu  
     325                   330                   335  
 Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp  
     340                   345                   350  
 Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser  
     355                   360                   365  
 Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu  
     370                   375                   380  
 Thr Arg Asp Pro Thr Thr Pro Xaa Thr Arg Ala Ala Trp Glu Thr Val  
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 Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala  
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 Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile  
     420                   425                   430  
 Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr  
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 Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu  
     450                   455                   460  
 Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His  
     465                   470                   475                   480  
 Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro  
     485                   490                   495  
 Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile  
     500                   505                   510  
 Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp  
     515                   520                   525

Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg  
530 535 540  
Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile  
545 550 555 560  
Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Cys Leu  
565 570 575  
Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg  
580 585 590

<210> 2  
<211> 1776  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> modified NS5B

<221> variation  
<222> (3)...(3)  
<223> n = A or T

<221> variation  
<222> (9)...(9)  
<223> n = C or A

<221> variation  
<222> (13)...(13)  
<223> n = A or T

<221> variation  
<222> (15)...(15)  
<223> n = A or C

<221> variation  
<222> (21)...(21)  
<223> n = A or G

<221> variation  
<222> (24)...(24)  
<223> n = C or G

<221> variation  
<222> (28)...(28)  
<223> n = T or C

<221> modified\_base  
<222> (30)...(30)  
<223> n = G or C

<221> variation  
<222> (33)...(33)  
<223> n = C or A

<221> variation  
<222> (71)...(71)

<223> n = A or G

<221> variation

<222> (83)...(83)

<223> n = G or T

<221> variation

<222> (1174)...(1174)

<223> n = A or C

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acctcgagga gtcctctct	gagggcaaag aaggtgactt	ttgacagggt gcaggtgctg	180
gacgcacact atgactcagt	cttgcaggac gttaagcggg	ccgcctctaa gtttagtgcg	240
aggctcctca cggtagagga	agcctgcgcg ctgacccgc	cccactccgc caaatcgcg	300
tacggatttg gggcaaaaaga	ggtgcgcagc ttatctagga	gggcccgttaa ccacatccgg	360
tccgtgtggg aggacctcct	ggaagaccaa cataccccaa	ttgacacacaac tatcatggct	420
aaaaatgagg tggctctgcat	tgatccaact aaagggtgggaa	aaaagccagc tcgcctcatc	480
gtataccccg accttgggt	cagggtgtgc gaaaagatgg	ccctctatga catcgaccaa	540
aagctccca aagcgataat	ggggccatcc tatgggttcc	aatactctcc cgcagaacgg	600
gtcgatttcc tcctcaaagc	ttggggaaagt aagaaggacc	caatgggtt ctcgtatgac	660
acccgctgct ttgactcaac	cgtcacggag agggacataa	gaacagaaga atccatatat	720
caggcttgtt ctctgcctca	agaagccaga actgtcatac	actcgctcac tgagagacatt	780
tacgttaggag ggcccatgac	aaacagcaaa gggcaatcct	gcggctacag gcgttgcgc	840
gcaagcgggt ttttaccac	cagcatgggg aataccatga	catgttacat caaagccctt	900
gcagcgtgta aggctgcagg	gatcgtggac cctgttatgt	tggtgtgtgg agacgacctg	960
gtcgtcatct cagagagcca	aggtAACGAG gaggacgagc	gaaacctgag agctttcacg	1020
gaggctatga ccaggatttc	cgcccctccc ggtgaccttc	ccagaccgga atatgacttg	1080
gagcttataa catcctgctc	ctcaaacgta tcggtagcgc	tggactctcg gggcgcgc	1140
cggtaacttcc taaccagaga	ccctaccact ccantcaccc	gagctgcttg ggaaacagata	1200
agacactccc ctgtcaattc	ttggctgggc aacatcatcc	agtacgcccc cacaatctgg	1260
gtccggatgg tcataatgac	tcacttcttc tccatactat	tggcccagga cactctgaac	1320
caaaatctca attttgagat	gtacggggca gtatactcgg	tcaatccatt agacctaccg	1380
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tgtggccgct acctcttcaa	ctggggcggtg aaaacaaagc	tcaaactcac tccattgccc	1620
gaggcgagcc gcctggattt	atccgggtgg ttcacctgtgg	gcccggcgg gggcgacatt	1680
tatcacagcg tgcgcatgc	ccgacccgc ctattactcc	tttgctact cctacttagc	1740
gtaggagtag gcatctttt	actccccat cgatga		1776

<210> 3

<211> 1394

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> VARIANT

<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT

&lt;222&gt; (904) ... (904)

&lt;223&gt; Xaa = valine or alanine

&lt;400&gt; 3

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Cys	Ile	Ile	Thr	Ser	Leu	Thr	Gly	Arg	Asp	Lys	Asn	Gln	Val	Glu	Gly
										25					30
Glu	Val	Gln	Val	Val	Ser	Thr	Ala	Thr	Gln	Ser	Phe	Leu	Ala	Thr	Cys
										40					45
Val	Asn	Gly	Val	Cys	Trp	Thr	Val	Tyr	His	Gly	Ala	Gly	Ser	Lys	Thr
										55					60
Leu	Ala	Gly	Pro	Lys	Gly	Pro	Ile	Thr	Gln	Met	Tyr	Thr	Asn	Val	Asp
										70					80
Gln	Asp	Leu	Val	Gly	Trp	Gln	Ala	Pro	Pro	Gly	Ala	Arg	Ser	Leu	Thr
										85					95
Pro	Cys	Thr	Cys	Gly	Ser	Ser	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala
										100					110
Asp	Val	Ile	Pro	Val	Arg	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu	
										115					125
Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu
										130					140
Leu	Cys	Pro	Ser	Gly	His	Ala	Val	Gly	Ile	Phe	Arg	Ala	Ala	Val	Cys
										145					160
Thr	Arg	Gly	Val	Ala	Lys	Ala	Val	Asp	Phe	Val	Pro	Val	Glu	Ser	Met
										165					175
Glu	Thr	Thr	Met	Arg	Ser	Pro	Val	Phe	Thr	Asp	Asn	Ser	Ser	Pro	Pro
										180					190
Ala	Val	Pro	Gln	Thr	Phe	Gln	Val	Ala	His	Leu	His	Ala	Pro	Thr	Gly
										195					205
Ser	Gly	Lys	Ser	Thr	Lys	Val	Pro	Ala	Ala	Tyr	Ala	Ala	Gln	Gly	Tyr
										210					220
Lys	Val	Leu	Val	Leu	Asn	Pro	Ser	Val	Ala	Ala	Thr	Leu	Gly	Phe	Gly
										225					240
Ala	Tyr	Met	Ser	Lys	Ala	His	Gly	Ile	Asp	Pro	Asn	Ile	Arg	Thr	Gly
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Val	Arg	Thr	Ile	Thr	Thr	Gly	Ala	Pro	Val	Thr	Tyr	Ser	Thr	Tyr	Gly
										260					270
Lys	Phe	Leu	Ala	Asp	Gly	Gly	Cys	Ser	Gly	Gly	Ala	Tyr	Asp	Ile	Ile
										275					285
Ile	Cys	Asp	Glu	Cys	His	Ser	Thr	Asp	Ser	Thr	Thr	Ile	Leu	Gly	Ile
										290					300
Gly	Thr	Val	Leu	Asp	Gln	Ala	Glu	Thr	Ala	Gly	Ala	Arg	Leu	Val	Val
										305					320
Leu	Ala	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Val	Thr	Val	Pro	His	Pro	Asn
										325					335
Ile	Glu	Glu	Val	Ala	Leu	Ser	Asn	Thr	Gly	Glu	Ile	Pro	Phe	Tyr	Gly
										340					350
Lys	Ala	Ile	Pro	Ile	Glu	Ala	Ile	Arg	Gly	Gly	Arg	His	Leu	Ile	Phe
										355					365
Cys	His	Ser	Lys	Lys	Lys	Cys	Asp	Glu	Leu	Ala	Ala	Lys	Leu	Ser	Gly
										370					380
Leu	Gly	Ile	Asn	Ala	Val	Ala	Tyr	Tyr	Arg	Gly	Leu	Asp	Val	Ser	Val
										385					400

Ile Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met  
 405 410 415  
 Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys  
 420 425 430  
 Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu  
 435 440 445  
 Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly  
 450 455 460  
 Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly  
 465 470 475 480  
 Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr  
 485 490 495  
 Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val  
 500 505 510  
 Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp  
 515 520 525  
 His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp  
 530 535 540  
 Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr  
 545 550 555 560  
 Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro  
 565 570 575  
 Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr  
 580 585 590  
 Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn  
 595 600 605  
 Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met  
 610 615 620  
 Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly  
 625 630 635 640  
 Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val  
 645 650 655  
 Ile Val Gly Arg Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp  
 660 665 670  
 Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser  
 675 680 685  
 His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys  
 690 695 700  
 Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala  
 705 710 715 720  
 Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp  
 725 730 735  
 Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly  
 740 745 750  
 Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe  
 755 760 765  
 Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe  
 770 775 780  
 Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala  
 785 790 795 800  
 Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser  
 805 810 815  
 Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala  
 820 825 830

Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met  
 835 840 845  
 Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro  
 850 855 860  
 Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His  
 865 870 875 880  
 Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala  
 885 890 895  
 Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu  
 900 905 910  
 Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile  
 915 920 925  
 Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser  
 930 935 940  
 Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys  
 945 950 955 960  
 Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro  
 965 970 975  
 Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly  
 980 985 990  
 Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala  
 995 1000 1005  
 Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro  
 1010 1015 1020  
 Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr  
 1025 1030 1035 1040  
 Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala  
 1045 1050 1055  
 Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly  
 1060 1065 1070  
 Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro  
 1075 1080 1085  
 Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg  
 1090 1095 1100  
 Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val  
 1105 1110 1115 1120  
 Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro  
 1125 1130 1135  
 Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp  
 1140 1145 1150  
 Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly  
 1155 1160 1165  
 Ser Pro Pro Ser Leu Ala Ser Ser Ala Ile Gln Leu Ser Ala Pro  
 1170 1175 1180  
 Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp  
 1185 1190 1195 1200  
 Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Xaa Ile  
 1205 1210 1215  
 Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp  
 1220 1225 1230  
 Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu  
 1235 1240 1245  
 Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala  
 1250 1255 1260

Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp  
 1265 1270 1275 1280  
 Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala  
 1285 1290 1295  
 Pro Pro Ile Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu  
 1300 1305 1310  
 Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly  
 1315 1320 1325  
 Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro  
 1330 1335 1340  
 Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr  
 1345 1350 1355 1360  
 Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser  
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 Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val  
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 Cys Cys

<210> 4  
 <211> 4182  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> modified NS3-5A

<221> variation  
 <222> (2711)...(2711)  
 <223> n = T or C

<221> variation  
 <222> (3645)...(3645)  
 <223> n = A or G

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